37. (Amended) A method of distinguishing a tumor type comprising determining the pattern of [9p] homozygous deletions in the MTAP gene having the sequence of SEQ ID NO:1 and associating the pattern with a pattern obtained from a tumor sought to be identified.

REMARKS

Status of the Claims:

Claims 2-6, 9 and 26-33 have been canceled. Claims 1, 7, 14, 15, 22, and 34-37 have been amended. Claim 1, 8, 10-25 and 34-38 are pending in the case.

Rejection of Claims under 35 U.S.C. §112, second paragraph:

Claims 7, 14 and 36 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. In claim 7, the term "standard hybridization conditions" is said to be unclear as there is no such thing according to the action as "standard" condition. Applicants have amended claim 7 to indicate that the conditions are those of high stringency. Conditions of high stringency are generally described in the specification on page 89, line 25. Conditions of high stringency are well known and practiced by those of skill in the art.

The preamble to claim 14 has been rejected as unacceptable. Applicants have amended the preamble of claim 14 in accordance with the examiner's suggestion to read "A method of making MTAP protein".

The meaning of the term "T98G" has been rejected as unclear for failing to provide specific characteristics of the DNA so described. Claim 36 has been amended to more clearly

define T98G. The characteristics of T98G are referred to in the specification on pages 52, 53, 56, 83 and 84.

Rejection of Claims 34 and 35 under 35 U.S.C. §101:

Claims 34 and 35 have been rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter *i.e.* to all endogenous or naturally occurring tumor suppresser genes on chromosome 9p21-22. Applicants have amended claims 34 and 35 to indicate that the tumor suppresser gene is identified as the nucleic and segment of claim 1.

Rejection of the Claims under 35 U.S.C. §102:

Claims 1-12, 15-18, 20-25 and 34-38 have been rejected under 35 U.S.C. §102(a) as anticipated by the Dreyling, *et al.* reference. Claims 1-12, 15-18, 20-25 and 34-38 have also been rejected under 35 U.S.C. §102(b) as anticipated by Nobori, *et al.* The claims have also been rejected as anticipated by Bohlander, *et al* .(1994).

The Olopade, *et al.* reference was published within one year of the filing of the present application. Applicants intend to submit a declaration indicating that authors Helen M. Pomykala, Fitsum Hagos, Lise W. Sveen, Rafael Espinosa, III, Martin H. Dreyling, Susan Gursky, Walter M. Stadler, Michelle M. Le Beau and Stefan K. Bohlander were not inventors of the claimed subject matter.

The Dreyling, *et al.* reference (1995) relates only to the use of FISH to detect deletions in the CDKN2 region of chromosomal band 9p21. This paper does not isolate or identify the MTAP gene encoding methylthioadenosine phosphorylase.

The Bohlander *et al.* paper (1994) refers only to the existence of the MTAP gene encoding methylthioadenosine phosphorylase. The paper reports certain deletion mapping results of studies relating to attempts to isolate and characterize tumor suppresser genes. As noted on page 215 of the publication, "The relative position on the map of the Not I site and the MTAP gene is uncertain at the present time." The publication itself, therefore, expressly indicates that the MTAP gene encoding methylthioadenosine phosphorylase has not been isolated and identified.

Claims 1-12, 15-18, 20-25 and 34-38 have been rejected under 35 U.S.C. §102(b):

Claims 1-12, 15-18, 20-25 and 34-38 have been rejected under 35 U.S.C. s102(b) as anticipated by Nobori, *et al.* (1994). The examiner's position is that Nobori, *et al.* disclosed MTAP, cDNA, gene in isolated regions designated T98G as well as kits and methods of use. However, as is evident from the abstract as well as the text of the publication, the author used deletion analysis and other procedures to isolate and characterize a putative tumor suppresser gene on chromosome 9p. The T98G glioma cell line was stated to have a deletion in 9p, nevertheless expressing methylthioadenosine phosphorylase. The CDK4 inhibitor gene was ultimately isolated and characterized. This is not the same gene that encodes methylthioadenosine phosphorylase.

Claims 1, 5, and 6 have been rejected under 35 U.S.C. §102(b):

Claims 1, 5, and 6 have been rejected under 35 U.S.C. s 102(b) as anticipated by the Chakraborti & Kozak (1992) reference. This reference discloses genes encoding microtubule

associated proteins known as MTAP. Applicants respectfully direct attention to the fact that these microtubule associated proteins are not in any manner related to or the same as methylthioadenosine phosphorylase protein. In fact, the families of microtubule associated protein genes studied by Chakraborti and Kozak map to chromosomes 1, 2, and 13. The MTAP gene encoding methylthioadenosine phosphorylase is found on chromosome 9p21.

Claims 13 and 14 have been rejected under 35 U.S.C. §102(b):

Claims 13 and 14 have been rejected under 35 U.S.C. §102(b) as anticipated by the Coffey, *et al.* reference (1994). The action draws attention to the microtubule associated proteins described in this publication. For the reasons discussed in relation to the Chakraborti and Kozak reference above, applicant respectfully requests withdrawal of this rejection as the microtubule associated proteins are in no way related to methylthioadenosine phosphorylase.

The rejection of various of claims 34-38 as anticipated by any one of Serrano, *et al.* (1993), Kamb, *et al.* (1994), Porterfield, *et al.* (1994), Porterfield, *et al.* (1992), Cheng, *et al.* (1994) or Scaleti, *et al.* (1987) is respectfully traversed. Serrano, *et al.* and Kamb, *et al.* disclose genes that are different from the MTAP gene characterized and identified in the present application. The 1992 Porterfield, *et al.* reference reports only that hybrids without an intact 9p continue to grow, suggesting the presence of a gene product that in normal cells would suppress tumor growth. The Porterfield references only identify tumor suppression activity with some as yet undefined deletions on human chromosome 9. The short arm of human chromosome 9 has

been recognized as including several genes', however, the work does not identify the absence of only the MTAP gene as associated with identification of a tumor type.

For the reasons stated, it is believed that the cited references do not disclose the MTAP gene or are not prior art with respect to the claimed subject matter.

Applicants intend this response to be a complete response to the examiner's action and early allowance is solicited.

The Examiner is invited to contact the undersigned attorney at 512-418-3108 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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